PARASITICIDE FORMULATIONS SUITABLE FOR DERMAL APPLICATION

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U.S. Cl. 514/341
Field of Search 514/452, 228, 514/341

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Attorney, Agent, or Firm—Joseph C. Gil; Godfried R. Akerli

ABSTRACT
The present invention relates to formulations for the dermal control of parasitic insects on animals, having the following composition:

- agonists or antagonists of the nicotinic acetylcholine receptors of insects in a concentration of from 1 to 20% by weight based on the overall weight of the formulation;
- solvents from the group benzyl alcohol or optionally substituted pyrrolidones in a concentration of at least 20% by weight based on the overall weight of the formulation;
- if desired, further solvents from the group consisting of cyclic carbonates or lactones in a concentration of from 5.0 up to 80% by weight based on the overall weight of the formulation;
- if desired, further auxiliaries from the group thickeners, spreading agents, colorants, antioxidants, propellants, preservatives, adhesives, emulsifiers, in a concentration of from 0.025 up to 10% by weight based on the overall weight of the formulation.

3 Claims, No Drawings
PARASITICIDE FORMULATIONS SUITABLE FOR DERMAL APPLICATION

This application is a 371 of PCT/EP95/04667 filed Nov. 27, 1995.

The present invention relates to formulations for the dermal control of parasitic insects on animals by means of agonists or antagonists of the nicotinic acetylcholine receptors of insects.

Agonists or antagonists of the nicotinic acetylcholine receptors of insects are known. They include the nicotinyl insecticides and, very particularly, the chloronicotinyl insecticides.

PCT application WO 93/24 002 discloses that certain 1-[(N-(halo-3-pyridylmethyl)]-N-methylanino-1-alkylamino-2-nitroethylene derivatives are suitable for systemic use against fleas in domestic animals. According to WO 93/24 002, the nonsystemic—i.e. dermal—mode of application is unsuitable for the control of fleas on domestic animals.

New formulations for the dermal application of agonists or antagonists of the nicotinic acetylcholine receptors of insects have now been found which are particularly suitable for dermal control of parasitic insects, such as fleas, lice or flies, on animals.

The formulations according to the invention have the following composition:

agonists or antagonists of the nicotinic acetylcholine receptors of insects in a concentration of from 1 to 20% by weight based on the overall weight of the formulation;

solvents from the group benzyl alcohol or optionally substituted pyrrolidones in a concentration of at least 20% by weight based on the overall weight of the formulation;

if desired, further solvents from the group consisting of cyclic carbonates or lactones in a concentration of from 5.0 up to 80% by weight based on the overall weight of the formulation;

if desired, further auxiliaries from the group thickeners, spreading agents, colorants, antioxidants, propellants, preservatives, adhesives, emulsifiers, in a concentration of from 0.025 up to 10% by weight based on the overall weight of the formulation.

Agonists or antagonists of the nicotinic acetylcholine receptors of insects are known, for example, from European Offenlegungsschriften (European Published Applications) Nos. 464 830, 428 941, 425 978, 386 565, 383 091, 375 907, 364 844, 315 826, 259 738, 254 859, 235 725, 212 600, 192 060, 163 855, 154 178, 136 636, 303 570, 302 833, 306 966, 189 972, 455 000, 135 956, 471 372, 302 389; German Offenlegungsschriften (German Published Specifications) Nos. 363 877, 3 712 307; Japanese Offenlegungsschriften (Japanese Published Applications) Nos. 03 220 176, 02 207 083, 63 307 857, 63 287 764, 03 246 283, 04 9371, 03 279 359, 03 255 072, U.S. Pat. Nos. 5,034,524, 4,948,798, 4,918,066, 5,039,686, 5,034,404; PCT Applications Nos. 91/17 659, 91/4965; French Application No. 2 611 114; Brazilian Application No. 88 03 621.

Express reference is hereby made to the compounds described in these publications and to their preparation.

These compounds can be represented preferably by the general formula (I)

\[
\begin{align*}
\text{R} & = \text{H, optionally substituted radicals from the group acyl, alkyl, aryl, aralkyl, heteroaryl or heteroarylalkyl; } \\
\text{A} & = \text{a monofunctional group from the series hydrogen, acyl, alkyl, aryl, or represents a bifunctional group which is linked to the radical Z; } \\
\text{E} & = \text{an electron-withdrawing radical; } \\
\text{X} & = \text{the radicals —CH= or —N=, it being possible for the radical —CH= instead of a H-atom to be linked to the radical Z; } \\
\text{Z} & = \text{a monofunctional group from the series alkyl, —O—R, —S—R, or represents a bifunctional group which is linked to the radical A or to the radical X.} \\
\end{align*}
\]

or represents a bifunctional group which is linked to the radical A or to the radical X.

Particularly preferred compounds of the formula (I) are those in which the radicals have the following meaning:

\[\text{R represents hydrogen and represents optionally substituted radicals from the series acyl, alkyl, aryl, or represents a bifunctional group which is linked to the radical A or to the radical Z.}
\]

\[\text{A represents a monofunctional group from the series alkyl, —O—R, —S—R, or represents a bifunctional group which is linked to the radical A or to the radical Z.}
\]

or represents a bifunctional group which is linked to the radical A or to the radical X.

Particularly preferred compounds of the formula (I) are those in which the radicals have the following meaning:

\[\text{R represents hydrogen and represents optionally substituted radicals from the series acyl, alkyl, aryl, or represents a bifunctional group which is linked to the radical A or to the radical Z.}
\]

\[\text{A represents a monofunctional group from the series alkyl, —O—R, —S—R, or represents a bifunctional group which is linked to the radical A or to the radical Z.}
\]
preferably fluorine, chlorine, bromine and iodine, especially fluorine, chlorine and bromine; cyano; nitro; amino; monoalkyl- and dialkylamino having preferably 1 to 4, in particular 1 or 2 carbon atoms per alkyl group, such as methylvamino, methyl-ethylamino, n- and i-propylamino and methyl-n-butylamino; carboxyl; carboxalkoxy having preferably 2 to 4, in particular 2 or 3 carbon atoms, such as carbomethoxy and carboxethoxy; sulpho (—SO₃H); alkylsulphonyl having preferably 1 to 4, in particular 1 or 2 carbon atoms, such as methylsulphonyl and ethylsulphonyl; arylsulphonyl having preferably 6 or 10 aryl carbon atoms, such as phenylsulphonyl, and also heteroarylamino and heteroaryalkylamino such as chloropyridylamino and chloropyridylimethylamino.

A particularly preferably represents hydrogen and represents optionally substituted radicals from the series acyl, alkyl, aryl, which preferably have the meanings given for R. A additionally represents a bifunctional group. There may be mentioned optionally substituted alkylene having 1–4, in particular 1–2 C atoms, substituents which may be mentioned being the substituents listed earlier above, and it being possible for the alkylene groups to be interrupted by heteroatoms from the series N, O, S.

A and Z may, together with the atoms to which they are attached, form a saturated or unsaturated heterocyclic ring. The heterocyclic ring can contain a further 1 or 2 identical or different heteroatoms and/or hetero-groups. Heteroatoms are preferably oxygen, sulphur or nitrogen, and hetero-groups are preferably N-alkyl, where the alkyl in the N-alkyl group preferably contains 1 to 4, in particular 1 or 2 carbon atoms. As alkyl there may be mentioned methyl, ethyl, n- and i-propyl and n-, i- and t-butyl. The heterocyclic ring contains 5 to 7, preferably 5 or 6 ring members.

Examples of the heterocyclic ring which may be mentioned are pyrrolidine, piperidine, piperazine, hexamethylenimine, morpholine and N-methylpiperazine.

As compounds which may be used with very particular preference in accordance with the invention, mention may be made of compounds of the general formulas (II) and (III):

\[
\text{(II)} \quad \text{subst.} - \begin{array}{c}
\text{CH}_2 - \text{N} - \text{(A)} - \text{(Z)} - \text{E} \\
/ \\
\text{N} \\
\end{array}
\]

\[
\text{(III)} \quad \text{subst.} - \begin{array}{c}
\text{CH}_2 - \text{N} - \text{(A)} - \text{(Z)} - \text{E} \\
/ \\
\text{N} \\
\end{array}
\]

in which

n represents 1 or 2,
subst. represents one of the above-listed substituents, especially halogen, very particularly chlorine,
A, Z, X and E have the meanings given above.

Specifically, the following compounds may be mentioned:

\[
\begin{align*}
\text{Cl} & - \text{N} - \text{CH}_2 - \text{N} - \text{(A)} - \text{(Z)} - \text{E} - \text{NO}_2 \\
\text{Cl} & - \text{N} - \text{CH}_2 - \text{N} - \text{(A)} - \text{(Z)} - \text{E} - \text{CH}_3 \\
\text{Cl} & - \text{N} - \text{CH}_2 - \text{N} - \text{(A)} - \text{(Z)} - \text{E} - \text{NH}_2 \\
\text{Cl} & - \text{N} - \text{CH}_2 - \text{N} - \text{(A)} - \text{(Z)} - \text{E} - \text{N}-\text{NO}_2 \\
\end{align*}
\]
The formulations according to the invention contain the active substance in concentrations of from 0.1 to 20% by weight, preferably from 1 to 12.5% by weight.

Preparations which are diluted before use contain the active substance in concentrations of from 0.5 to 90% by weight, preferably from 1 to 50% by weight.

In general, it has proved to be advantageous to administer quantities of from about 0.5 to about 50 mg, preferably from 1 to 20 mg, of active substance per body weight per day in order to achieve effective results.

Suitable solvents are:

- benzyl alcohol or optionally substituted pyrrolidones such as 2-pyrrolidone, 1-(C_{12-20}-alkyl)-2-pyrrolidone, in particular 1-ethylpyrrolidone, 1-octylpyrrolidone, 1-dodecylpyrrolidone, 1-isopropylpyrrolidone, 1-(s- or t- or n-butyl)pyrrolidone, 1-hexylpyrrolidone, 1-(C_{2-20}-alkenyl)-2-pyrrolidone such as 1-vinyl-2-pyrrolidone, 1-(C_{3-8}-cycloalkyl)-2-pyrrolidone such as 1-cyclohexylpyrrolidone, 1-(C_{1-6}-hydroxyalkyl)-2-pyrrolidone, 1-(C_{1-6}-alkoxy-C_{1-6}-alkyl)-2-pyrrolidone such as 1-(2-hydroxyethyl)-pyrrolidone, 1-(3-hydroxypropyl)pyrrolidone, 1-(2-methoxyethyl)-pyrrolidone, 1-(3-methoxypropyl)-pyrrolidone, and also 1-benzylpyrrolidone. Particular
mention may be made of benzyl alcohol or n-dodecyl- or n-octylpyrrolidone. These solvents can be employed either alone or in a mixture with additional solvents (cosolvents). They are present in a concentration of at least 20% by weight; preferably from 40 to 90% by weight, particularly preferably from 50 to 90% by weight.

Suitable additional solvents or cosolvents are: cyclic carbonates or lactones. As such there may be mentioned: ethylene carbonate, propylene carbonate, γ-butyrolactone.

They are present in a concentration from 50.0 up to 80% by weight, preferably from 7.5 to 50% by weight, particularly preferably from 10 to 50% by weight.

Suitable further auxiliaries are: preservatives such as benzyl alcohol (not required if already present as solvent), trichlorobutanol, p-hydroxybenzoic esters, n-butanol.

Thickeners such as: inorganic thickeners such as bentonites, colloidal silicic acid, aluminium monostrate, organic thickeners such as cellulose derivatives, polyvinyl polylactones, polyvinylpyrrolidones and copolymers thereof, acrylates and methacrylates.

Colorants which may be mentioned are all colorants where use on the animal is permitted, which may be dissolved or suspended.

Auxiliaries are also spreading oils such as di-2-ethylhexyl adipate, isopropyl myristate, dipropylene glycol pelargonate, cyclic and acyclic silicone oils such as dimeticones and also co- and terpolymers thereof with ethylene oxide, propylene oxide and formalin, fatty acid esters, triglycerides, fatty alcohols.

Antioxidants are sulphites or metabisulphites such as potassium metabisulphite, a scorbic acid, butylated hydroxytoluene, butylated hydroxyanisole, tocopherol.

Light stabilizers are, for example, substances from the class of the benzophenones or Novanisic acid.

Adhesives are, for example, cellulose derivatives, starch derivatives, polyacrylates, naturally occurring polymers such as alginites, gelatin.

Auxiliaries are also emulsifiers such as nonionic surfactants, for example polyoxyethylated castor oil, polyoxyethylated sorbitan monooleate, sorbitan monostrate, glycerol monostrate, polyoxyethylated alkanol, alkylphenol polyglycol ethers;

ampholytic surfactants such as di-Na lauryl-β-

inmonopropionate or lecinthin;

anionic surfactants, such as Na-lauryl sulphate, fatty alcohol ether sulphates, mono/dialkylpolyglycol ether orthophosphoric ester monooethanolamine salt; cationic surfactants such as cetlytrimethylammonium chloride.

Further auxiliaries are agents with which the formulations according to the invention can be sprayed or squirted onto the skin. These are the conventional propellent gases required for spray cans, such as propane, butane, dimethyl ether, CO₂ or halogenated lower alkanes, or mixtures thereof with one another.

While being of low toxicity to warm-blooded species, the formulations according to the invention are suitable for the control of parasitic insects which are encountered in animal keeping and animal breeding in domestic and productive animals and in zoo and laboratory animals and animals used for experimentation and in the pursuit of hobbies. In this context they are active against all or individual stages of development of the pests and against resistant and normally sensitive species of the pests.

The pests include:


Particular mention may be made of the action against Siphonaptera, especially against fleas.

The productive and breeding animals include mammals such as, for example, cattle, horses, sheep, pigs, goats, camels, water buffalo, donkeys, rabbits, fallow deer, reindeer, fur-bearing animals such as, for example, mink, chinchilla or racoon, birds such as, for example, chickens, geese, turkeys, ducks.

Laboratory animals and those for experimentation include mice, rats, guinea pigs, golden hamsters, dogs and cats.

The hobby animals include dogs and cats.

Administration can be effected both prophylactically and therapeutically.

In the shaped articles according to the invention, it is also possible for further active substances to be present. The further active substances include insecticides such as phosphorus-containing compounds, i.e. phosphates or phosphonates, natural or synthetic pyrethroids, carbamates, amidines, juvenile hormones and juweind synthetic active substances, and chitin synthesis inhibitors such as diaryl ethers and benzoylureas.

The phosphates or phosphonates include:

-0-ethyl-0(8-quino)xyphenylphenyl thiophosphate (quintiofos),
-0,0-dietyl 0-(3-chloro-4-methyl-7-coumarinyl)- thiophosphate (coumaphos),
-0,0-dietyl 0-phenylglyoxylonitrile oxime thiophosphate (phoxim),
-0,0-dietyl 0-cyanochlorobedoxime thiophosphate (chloroprim),
-0,0-dietyl 0(4-brom2,5-dichlorophenyl) phosphorothioi-
die (bromophos-ethyl),
-0,0,0′-tetraethyl S,S-methylene-di(phosphorodihiolate) (ethion),
-2,3-p-di oxanedithiol S,S-bis(0,0-dietyl phosphorodihiolate),
-2-chloro-1-(2,4-dichlorophenyl)-vinyl diethyl phosphate (chlorfenvitnphos),
-0,0-dimetil 0-(3-methyl-4-methylthiophenyl) thionophos-
phate (fenthion).

The carbamates include:

-2-isopropoxycarbonyl methylcarbamate (propxorin),
-1-naphthyl N-methylcarbamate (carbaryl).

The synthetic pyrethroids include
-3-[2-(4-chlorophenyl)-2-chlorovinyl]-2,2-dimethyl-cyclo-
propyloxyacetic acid (cyano-4-fluoro-3-phenoxy)-
benzyl ester (Flumethrin),
-cyano-4-fluoro-3-phenoxy)-benzyl 2,2-dimethyl-3-(2,2-
dichlorovinyl)-cyclopropyloxyacetic acid (cyfluthrin) and its enantiomers and stereomers,
-cyano-3-phenoxybenzyl (±)-cis, trans-3-(2,2-
dichlorovinyl) 2,2-dimethylocyclopropyloxyacetyl-
(dealtamethrin),
-cyano-3-phenoxybenzyl 2,2-dimethyl-3-(2,2-
dichlorovinyl)-cyclopropyloxyacetyl (cypermethrin),
3-phenoxypybenzyl (E)-cis, trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (permethrin),
cyano-3-phenoxypybenzyl (p-Cl-phenyl)-isovalerate (fenvalerate),
2-cyano-3-phenoxypybenzyl 2-(2-chloro- , trifluoro-p-toluidino)-3-methylbutyrate (flualinate).

The amidines include:
3-methyl-2-[2,4-dimethyl-phenylimino]-thiazoline,
2-(4-chloro-2-methylphenylimino)-3-methylthiazolidine,
2-(4-chloro-2-methylphenylimino)-3-(isobutyl-1-enyl)-thiazolidine
1,5-bis-(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene (amitraz).

Cyclic macroliths such as invermectins and abamectins.
In this context there may be mentioned, for example, 5-m0-dimethyl-22,23-dihydroavermetin-A_1,a, 22,23-
dihydroavermetin B_{1a} and 22,23-dihydroavermetin B_{2a} (cf. for example WHO).

F.A Series 27, pp. 27–73 (1991)). The juvenile hormones and juvenile hormone-like substances include, in particular,
compounds of the following formulae:

The substituted dial ethers include, in particular

The benzoyl ureas include compounds of the formula

The triazincinclus compounds of the formula
### EXAMPLE 3
Imidacloprid 8.5 g

n-dodecyl-pyrrolidone 45.25 g

γ-butyrolactone 45.25 g

@ Belsil L 066 1 g

(Polysiloxane copolymer as spreading agent)

### EXAMPLE 4
Imidacloprid 10 g

Benzyl alcohol 89.9 g

@ Belsil DMC 6031 0.1 g

(Polysiloxane copolymer as spreading agent)

### EXAMPLE 5
Imidacloprid 12.5 g

Benzyl alcohol 70.0 g

propylene carbonate 17.5 g

### EXAMPLE 6
Imidacloprid 10.0 g

1-cyclohexylpyrrolidone 80.0 g

Propylene carbonate 10.0 g

### EXAMPLE 7
Imidacloprid 11.0 g

Benzyl alcohol 70.0 g

Propylene carbonate 17.5 g

Isopropyl myristate 4.0 g

### EXAMPLE 8
Imidacloprid 12.5 g

Benzyl alcohol 70.0 g

Propylene carbonate 17.4 g

Butylated hydroxytoluene 0.1 g

### EXAMPLE 9
Imidacloprid 10.0 g

Benzyl alcohol 70.0 g

Propylene carbonate 17.5 g

Di-2-ethylhexyl adipate 2.5 g

### EXAMPLE 10
Imidacloprid 12.5 g

2-pyrrolidone 70.0 g

Propylene carbonate 17.5 g

### Example 1

<table>
<thead>
<tr>
<th>Substance</th>
<th>Amount</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imidacloprid</td>
<td>10 g</td>
<td>Belsil DMC 6031</td>
</tr>
<tr>
<td>Propylene carbonate</td>
<td>45 g</td>
<td></td>
</tr>
<tr>
<td>Benzyl alcohol</td>
<td>45 g</td>
<td></td>
</tr>
</tbody>
</table>

(A polysiloxane copolymer from Wacker GmbH, D-81737 Munich)

### Example 2

<table>
<thead>
<tr>
<th>Substance</th>
<th>Amount</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imidacloprid</td>
<td>10 g</td>
<td>Belsil L 066</td>
</tr>
<tr>
<td>n-octyl-2-pyrrolidone</td>
<td>44.5 g</td>
<td></td>
</tr>
<tr>
<td>γ-butyrolactone</td>
<td>44.5 g</td>
<td></td>
</tr>
</tbody>
</table>

(A polysiloxane copolymer from Wacker GmbH, D-81737 Munich)
**EXAMPLE 11**

<table>
<thead>
<tr>
<th>Imidacloprid</th>
<th>10.0 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyriproxyfen</td>
<td>1.0 g</td>
</tr>
<tr>
<td>Benzyl alcohol</td>
<td>70.0 g</td>
</tr>
<tr>
<td>Propylene carbonate</td>
<td>18.9 g</td>
</tr>
<tr>
<td>Butylated hydroxytoluene</td>
<td>0.1 g</td>
</tr>
</tbody>
</table>

**EXAMPLE 12**

| Imidacloprid | 12.5 g |
| Tribufon | 2.5 g |
| Benzyl alcohol | 60.0 g |
| Propylene carbonate | 27.5 g |

**EXAMPLE 13**

| Imidacloprid | 10.0 g |
| Flumeturin | 2.0 g |
| Benzyl alcohol | 60.0 g |
| Propylene carbonate | 28.0 g |

**EXAMPLE 14**

| Imidacloprid | 10.0 g |
| Benzyl alcohol | 60.0 g |
| Ethylene carbonate | 15.0 g |
| Propylene carbonate | 15.0 g |

**USE EXAMPLE A**

2 ml of the formulation described in Example 1 was poured onto the back of a dog weighing 20 kg which was infested with fleas. The following results were obtained:

<table>
<thead>
<tr>
<th>Period of time</th>
<th>Number of fleas per dog</th>
<th>% Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>Untreated</td>
<td>Treated</td>
</tr>
<tr>
<td>1 Infestation with 100 fleas</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>5, 8 Infestation with 100 fleas</td>
<td>56</td>
<td>0</td>
</tr>
<tr>
<td>9 Counting</td>
<td>76</td>
<td>0</td>
</tr>
<tr>
<td>15 Infestation with 100 fleas (untreated animals)</td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td>20 Counting</td>
<td>43</td>
<td>0</td>
</tr>
</tbody>
</table>

**USE EXAMPLE B**

1 ml of the solution according to Example 4 was placed on the shoulders of a dog weighing 20 kg. The animal was infested with 200 fleas after 2 and after 6 days of treatment. On day 3 and on day 7, respectively, of the treatment, the fleas remaining on the dog were counted. No living fleas were found. The action was 100%.

we claim:

1. A composition for the dermal control of parasitic insects on animals comprising: an agonist or antagonist of the nicotinergic acetylcholine receptors on insects in a concentration of from about 1% to about 20% by weight based on the overall weight of the composition comprising effective amount of the compound;

2. The composition according to claim 1 wherein the auxiliary is selected from the group consisting of thickeners, spreading agents, colorants, antioxidants, preservatives, adhesives, and emulsifiers;

3. A method for the dermal control of parasitic insects on animals, comprising applying to an animal in need thereof a physiologically active amount of the composition according to claim 1.
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 14, Lines 36-37
“and optionally an additional solvent” should be
--and an additional solvent--

Column 14, Line 43
“emulsit.” should be
--emulsifiers.--

Signed and Sealed this
Sixth Day of December, 2011

David J. Kappos
Director of the United States Patent and Trademark Office
EX PARTE REEXAMINATION CERTIFICATE (9477th)

United States Patent
Sirinyan et al.

Number: US 6,001,858 C1

PARASITICIDE FORMULATIONS SUITABLE FOR DERMAL APPLICATION

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Assignee: Bayer Animal Health GmbH, Leverkusen (DE)

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Filed: Jun. 2, 1997

Certificate of Correction issued Dec. 6, 2011.

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PCT Pub. Date: Jun. 13, 1996

Foreign Application Priority Data
Dec. 9, 1994 (DE) 44 43 888

References Cited

To view the complete listing of prior art documents cited during the proceeding for Reexamination Control Number 90/011,685, please refer to the USPTO’s public Patent Application Information Retrieval (PAIR) system under the Display References tab.

Primary Examiner — Evelyn Huang

ABSTRACT

The present invention relates to formulations for the dermal control of parasitic insects on animals, having the following composition agonists or antagonists of the nicotinic acetylcholine receptors of insects in a concentration of from 1 to 20 % by weight based on the overall weight of the formulation; solvents from the group benzyl alcohol or optionally substituted pyrrolidones in a concentration of at least 20 % by weight based on the overall weight of the formulation; if desired, further solvents from the group consisting of cyclic carbonates or lactones in a concentration of from 5.0 up to 80 % by weight based on the overall weight of the formulation; if desired, further auxiliaries from the group thickeners, spreading agents, colorants, antioxidants, propellants, preservatives, adhesives, emulsifiers, in a concentration of from 0.025 up to 10 % by weight based on the overall weight of the formulation.
EX PARTE
REEXAMINATION CERTIFICATE
ISSUED UNDER 35 U.S.C. 307

THE PATENT IS HEREBY AMENDED AS
INDICATED BELOW.

Matter enclosed in heavy brackets [ ] appeared in the
patent, but has been deleted and is no longer a part of
the patent; matter printed in italics indicates additions made
to the patent.

AS A RESULT OF REEXAMINATION, IT HAS BEEN
DETERMINED THAT:

Claim 1 is determined to be patentable as amended.

Claims 2-3, dependent on an amended claim, are
determined to be patentable.

New claims 4-22 are added and determined to be
patentable.

1. A composition for the dermal control of parasitic insects
on animals comprising: an agonist or antagonist of the
nicotinic acetylcholine receptors on insects in a concentration
of from about 1% to about 20% by weight based on the overall
weight of the composition comprising an effective amount of the
compound;

![Chemical Structure](image)

a solvent selected from the group consisting of benzyl alco-
hol and optionally substituted pyrrolidones selected from the
group consisting of 2-pyrrolidone, 1-(C\textsubscript{2,3,4,5}-aryl)-2-
pyrrolidone, 1-(C\textsubscript{2,3,4,5}-alkenyl)-2-pyrrolidone, 1-(C\textsubscript{2,3,4,5}-cycloalkyl)-
2-pyrrolidone, 1-(C\textsubscript{2,3,4,5}-hydroxyalkyl)-2-pyrrolidone, 1-
(C\textsubscript{2,3,4,5}-alkoxy-C\textsubscript{2,3,4,5}-alkyl)-2-pyrrolidone, and 1-benzylpyrrol-
done in a concentration of from 5.0 up to
80% by weight based on the overall weight of the composition, and an
additional solvent selected from the group consisting of cyclic
carbonates and lactones in a concentration of from 5.0 up to
80% by weight based on the overall weight of the composi-
tion, and an auxiliary selected from the group consisting of
thickeners, spreading agents, colorants, antioxidants, propel-
lants, preservatives, adhesives, and emulsifiers.

4. The method of claim 3, wherein said composition is
administered onto the back or shoulders of said animal.

5. The method of claim 3, wherein said dermal control is
effective for a period of at least up to 27 days.

6. The method of claim 3, wherein said additional solvent is
cyclic carbonate in a concentration of from 5.0 up to 80% by
weight based on the overall weight of the composition.

7. The method of claim 3, wherein said composition comprises a benzyl alcohol in a concentration of at least 20 to
90% by weight based on the overall weight of the composi-
tion.

8. The method of claim 3, wherein said composition comprises a benzyl alcohol in a concentration of at least 20 to
90% by weight based on the overall weight of the composi-
tion.

9. The method of claim 7, wherein said additional solvent is
cyclic carbonate in a concentration of from 5.0 up to 80% by
weight based on the overall weight of the composition.

10. The method of claim 9, wherein said cyclic carbonate is
propylene carbonate.

11. The method of claim 3, wherein said animal is a warm
blooded animal.

12. The method of claim 3, wherein said animal is a cat or
dog wherein said parasitic insects are fleas.

13. The method of claim 12, wherein the composition com-
prises from 1 to 12.5% by weight of the compound, from 50 to
90% by weight of benzyl alcohol, and from 10 to 50% by
weight of propylene carbonate.

14. The method of claim 3, wherein the composition further
comprises pyriproxyfen.

15. The method of claim 13, wherein the composition fur-
ther comprises pyriproxyfen.

16. The composition of claim 1, comprising a benzyl alco-
hol in a concentration of at least 20% to 90% by weight based
on the overall weight of the composition.

17. The composition of claim 1, wherein said additional
solvent is a cyclic carbonate in a concentration of from 5.0 up
to 80% by weight based on the overall weight of the composi-
tion.

18. The composition of claim 16, wherein said additional
solvent is a cyclic carbonate in a concentration of from 5.0 up
to 80% by weight based on the overall weight of the composi-
tion.

19. The composition of claim 18, wherein said cyclic car-
bonate is propylene carbonate.

20. The composition of claim 1, further comprising
pyriproxyfen.

21. The composition of claim 1, comprising from 1 to
12.5% by weight of the compound, from 50 to 90% by weight
of benzyl alcohol, and from 10 to 30% by weight of propylene
carbonate.

22. The composition of claim 21, further comprising
pyriproxyfen.

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